510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:
k061673

B. Purpose for Submission:
Addition of amoxicillin-clavulanate to the BD Phoenix™ Automated Microbiology System

C. Measurand:
Amoxicillin-clavulanate 0.25/0.12 – 32/16 µg/mL

D. Type of Test:
Antimicrobial Susceptibility Test (AST) (Qualitative) colorimetric oxidation-reduction, growth-based

E. Applicant:
Becton, Dickinson & Company

F. Proprietary and Established Names:
BD Phoenix™ Automated Microbiology System – Amoxicillin-clavulanate 0.25/0.12 – 32/16 µg/mL

G. Regulatory Information:

1. Regulation section:
   21 CFR 866.1645 Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System

2. Classification:
   II

3. Product code:
   LON System, Test, Automated, Antimicrobial Susceptibility, Short Incubation

4. Panel:
   83 Microbiology

H. Intended Use:

1. Intended use(s):
   Amoxicillin-clavulanate at 0.25/0.12 – 32/16 µg/mL on the Phoenix™ Gram Positive ID/AST or AST only panel is intended for use with the BD Phoenix Automated Microbiology System for *in vitro* quantitative determination of

antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most Gram-negative aerobic and facultative anaerobic bacteria isolates from pure culture for *Enterobacteriaceae* and non – *Enterobacteriaceae* and most Gram-positive bacteria isolates from pure culture belonging to the genera *Staphylococcus* and *Enterococcus*.

2. Indication(s) for use:
   This application is indicated for the addition of the antimicrobial agent amoxicillin-clavulanate at concentrations of 0.25/0.12 – 32/16 µg/mL to Gram-positive ID/AST or AST for testing *Staphylococcus* spp. and *Enterococcus* spp.

3. Special conditions for use statement(s):
   For prescription use only

4. Special instrument requirements:
   Not Applicable

I. Device Description:

The BD Phoenix™ Automated Microbiology System includes instrumentation and software, sealed and self-inoculating molded polystyrene trays with 136 micro-wells containing dried reagents, and specific inoculum broth formulations for ID and AST Indicator. The organism to be tested must be a pure culture and be preliminarily identified as gram positive or gram negative. Colonies are then suspended in broth, and equated to a 0.5 McFarland with the recommendation to use the BD CrystalSpec™ Nephelometer. A further dilution is made into an AST broth, which contains an AST indicator, prior to inoculating the panel. The AST broth is a cation-adjusted formulation of Mueller-Hinton broth containing 0.01% Tween 80. After adding the indicator solution to the AST inoculum the color is blue and after inoculation and incubation changes to pink then to colorless as reduction in the panel well proceeds. Inoculated panels are barcode scanned and loaded into the BD Phoenix™ Automated Microbiology System instrument where the panels are continuously incubated at 35^0C. The AST has a final inoculum of 5 x 10^5 CFU/ml. The instrument incubates, reads and records the results of the biochemical substrates and antimicrobial agents and interprets the reactions to give an ID of the isolate and MIC value and category interpretation of the antimicrobial agents. Organisms growing in the presence of a given antimicrobic agent reduce the indicator, signaling organism growth and resistance to the antimicrobic agent. Organisms killed or inhibited by a given antimicrobic do not cause reduction of the indicator and therefore do not produce a color change. Additional interpretation is done using software driven "EXPERT" System using rules derived from the NCCLS documentation.

Readings are taken every 20 minutes with an ID result available between 2-12 hours and an AST result available between 4-16 hours. This is only an autoread result; there are no manual readings possible.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   VITEK® System

2. Predicate 510(k) number(s):
   N50510

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
1. Intended Use	Intended for the *in vitro* rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most bacteria.	Same
2. Isolates	Isolated colonies from culture used	Isolated colonies from culture used
3. Result Reported	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)
4. Incubation Time	<16 hours	<16 hours
5. Type of Test	Automated	Automated

Differences		
Item	Device	Predicate
1. Results achieved	Results are determined from serial twofold dilutions of antimicrobial agents	Results are determined from extrapolation of doubling dilutions
2. Sample Preparation	Inoculum density equated to 0.5 McFarland standard	Inoculum density equated to 1.0 McFarland standard
3. Technology	Automated growth based enhanced by use of a redox indicator (colorimetric oxidation-reduction) to detect organism growth.	Automated growth based with detection using an attenuation of light measured by an optical scanner.

K. Standard/Guidance Document Referenced (if applicable):

"Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA"; CLSI M7 (M100-S16) "Methods for

Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard."

L. Test Principle:

The system employs conventional, colorimetric, fluorogenic and chromogenic substrates to identify the genus and species of the isolate. The AST portion of the BD Phoenix™ Automated Microbiology System is a broth based microdilution method that utilizes a redox indicator (colorimetric oxidation-reduction) to enhance detection of organism growth. The MIC is determined by comparing growth in wells containing serial two-fold dilutions of an antibiotic to the growth in "growth control wells" which contains no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Twenty seven isolates were evaluated for site to site and inter site reproducibility demonstrating >95% reproducibility. The ten isolate study described in the guidance document was used (10 organisms tested 3 times on 3 days at 3 sites).

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The FDA and CLSI recommended QC isolates, *E. faecalis* ATCC 29212 and *S. aureus* ATCC 29213 were tested on every test occasion with the reference method and the BD Phoenix™. The reference method QC results were in range for every day tested. The Phoenix™ was tested a sufficient number of times to demonstrate that the system can produce QC results in the CLSI recommended ranges most of the time. The mode of the *E. faecalis* QC with the reference method was 1 dilution lower than the test method.

Amoxicillin-Clavulanate Gram Positive QC Table

ORGANISM	**conc. (µg/mL)**	**Reference**	**BD Phoenix™**
E. faecalis ATCC 29212 Expected Range: ≤1 µg/mL	≤0.25	11	
	0.5	148	5
	1	4	107
	2	2	
S. aureus ATCC 29213 Expected Range: ≤0.5 µg/mL	≤0.25	22	7
	0.5	143	104

Inoculum density control: The organism suspension density of the ID broth was equivalent to a 0.5 McFarland standard using the BBL™ CrystalSpec™ Nephelometer which was verified each day of testing. Internal data was used to demonstrate that the use of the BBL™ CrystalSpec™ Nephelometer would produce reproducible results. Five different instruments were used.

d. Detection limit:
Not Applicable

e. Analytical specificity:
Not Applicable

f. Assay cut-off:
Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:
The CLSI recommended broth dilution reference panel was prepared according to the CLSI recommendation. Clinical testing was performed at four sites. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. The test device had a growth rate of >95%. A comparison was provided to the reference method with the following agreement.

GP Accuracy Summary Clinical and Challenge with MRS Removed

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Clinical	**820**	**769**	**93.8**	**580**	**555**	**95.7**	**791**	**96.5**	**188**	**N/A**	**23**	**6**
Challenge	**51**	**51**	**100**	**25**	**25**	**100**	**51**	**100**	**9**	**N/A**	**0**	**0**
Combined	**871**	**820**	**94.1**	**605**	**580**	**95.9**	**842**	**96.7**	**197**	**N/A**	**23**	**6**

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates
maj-major discrepancies
vmj-very major discrepancies
N/A – No minor errors possible since there is no intermediate category

Essential agreement (EA) is when the BD Phoenix™ panels agree with the reference test panel results exactly or within one doubling dilution of the reference method. Category agreement (CA) is when the BD Phoenix™ panel result interpretation (SIR) agrees exactly with the reference panel result interpretation. Evaluable EA is when the MIC result is on scale for both the BD Phoenix™ and the reference and have on-scale EA.

Also tested in the clinical study were 484 Methicillin Resistant *Staphylococci*

(MRS). However, MRS will be reported as amoxicillin/clavulanate resistant regardless of MIC value but the ability of the BD Phoenix™ to detect resistance in this group accurately demonstrates that the 1 vmj for the Methicillin Susceptible *Staphylococcus* (MSS) group would be acceptable. The maj error and vmj error rates for the MSS group are both acceptable.

There appears to be a trend with the *Enterococcus* spp. where the test device is more resistant than the reference method. This was observed in the QC and clinical studies. Also, the maj error rate for the *Enterococcus* spp. group of 4.0% was higher than as recommended in the guidance document but these recommendations are based on errors that would include a minor error range. Since this antibiotic has only a Sensitive (S) and a Resistant (R) result, all errors are either vmj or maj with no minor errors possible. However, if those errors that are in EA are removed, the maj rate of 2.7% (8/298) is acceptable. The vmj error rate for the *Enterococcus* spp. group is acceptable.

b. Matrix comparison:
Not Applicable

3. Clinical studies:

a. Clinical Sensitivity:
Not Applicable

b. Clinical specificity:
Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):
Not Applicable

4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range:
Staphylococcus ≤4/2(S), ≥8/4(R)
Enterococcus ≤8/4(S), ≥16/8(R)

N. Proposed Labeling:

The expected value range, interpretive criteria and QC for gram positive panels are included in the package insert. The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.